

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 12-15, 17-22, and 39-48 are pending and are directed to an amino acid (claims 12-15, 17-21, and 39-43) or a pharmaceutical formulation comprising the amino acid (claims 22 and 44-48).

*Amendments to the Claims*

Claims 1-11 and 23-38 have been canceled as directed to non-elected subject matter in response to the restriction requirement. The remaining claims have been amended to point out more particularly and claim more distinctly the invention.

In particular, claim 12 has been amended to incorporate the subject matter of claims 16-18. Claim 16 has been canceled, and claims 17 and 18 have been amended, in view of the amendment of claim 12. Claim 19 has been amended to change the dependence from claim 16 to claim 12 in view of the cancellation of claim 16. Claim 22 has been amended to delete the phrase "wherein R<sup>14</sup> comprises a carrier molecule that is a member selected from therapeutic moieties" in view of the amendment of claim 12. Minor grammatical changes have been made to claims 39 and 40.

New claim 41 recites that the amino acid of claim 12 has a specific structure as disclosed in the specification at paragraph 0122. New claim 42 recites that the amino acid of claim 12 has a specific structure as disclosed in the specification at paragraph 0118, and new claim 44 recites that the L variable of claim 43 comprises an -NH- moiety. Support for the definitions of the R<sup>15</sup>, L, and n variables as recited in claims 42 and 43 is found in the specification at, for example, paragraphs 0015, 0025, 0028, 0079, and 0104.

New claims 44-48 are similar to originally filed claim 22 except dependent on claims 17, 18, and 41-43, respectively.

No new matter has been added by way of the amendments to the claims.

*The Office Action*

Claims 1-11 and 23-38 have been withdrawn from consideration as being directed to non-elected subject matter in response to the restriction requirement.

Claims 12-15, 22, 39, and 40 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Claims 12, 13, 16, 17, 22, 39, and 40 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Kozlowski (U.S. Patent 6,376,604).

Claims 14 and 15 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Kozlowski in view of Sheridan (*J. Chem. Inf. Comput. Sci.*, 42: 103-108 (2002)).

Claims 18-21 have been objected to as being dependent upon a rejected base claim, but the Office Action indicates that claims 18-21 would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims.

Reconsideration of these rejections in view of the amendments and remarks set forth herein is respectfully requested.

*Discussion of Rejection Under 35 U.S.C. § 112*

Claims 12-15, 22, 39, and 40 have been rejected as allegedly being indefinite. Specifically, the Office contends that the phrases “reactive functional group” and “a group that is linked to a carrier molecule” recited for the R<sup>14</sup> group render the claims indefinite because the phrases allegedly do not convey a chemical structure. The aforementioned allegedly indefinite phrases have been deleted from claim 12, and claim 12 has been amended to recite that “R<sup>14</sup> is a nucleotide sugar or comprises a saccharide moiety conjugated to a member selected from a peptide and a lipid.” Claims 13-15, 22, 39, and 40 depend from claim 12 either directly or indirectly. Accordingly, Applicant respectfully submits that the amended claims are sufficiently clear, and requests withdrawal of the indefiniteness rejection.

*Discussion of Rejection Under 35 U.S.C. § 102(b)*

Claims 12, 13, 16, 17, 22, 39, and 40 have been rejected as allegedly anticipated by Kozlowski. Specifically, the Office contends that Kozlowski discloses amino acid derivatives formed by the reaction of 1-benzotriazolylcarbonate (BTC) esters of water-soluble polymers with amino acids. The Office states that an exemplary amino acid derivative disclosed in Kozlowski is a doubly PEGylated lysine. The Office also contends

that Kozlowski discloses the use of PEG having a molecular weight of from about 200 Da to about 100,000 Da and that the BTC esters of water-soluble polymers can be reacted with biologically active agents including small molecule drugs, nucleosides, and oligonucleotides.

Claim 12 has been amended to recite that  $R^{14}$  (a) comprises a saccharide moiety conjugated to a member selected from a peptide and a lipid or (b) is a nucleotide sugar. Claims 12-15, 19-22, and 39-43 are directly or indirectly dependent on claim 12.

Claim 18, which was dependent on claim 12 through intervening claim 16 was not subject to any rejection. As indicated above, the elements of claims 16 and 18 (i.e., that  $R^{14}$  comprises a saccharide moiety conjugated to a member selected from a peptide and a lipid) have been incorporated into claim 12. Thus, the anticipation rejection is inapplicable to definition “(a)” of the  $R^{14}$  variable as recited in amended claim 12.

The Office contends that claim 17, which was dependent on claim 12 through intervening claim 16, is anticipated by Kozlowski. Kozlowski discloses that “the invention involves the reaction of BTC esters of water-soluble and non-peptidic polymers with amino acids to form amino acid derivatives” (column 6, lines 43-45), such as doubly PEGylated lysine. Kozlowski also discloses that “BTC esters of water-soluble and non-peptidic polymers can also be reacted with biologically active agents to form biologically active polymer conjugates” (column 7, lines 8-10). According to Kozlowski, “[e]xamples of biologically active agents include ... small molecule drugs, ... nucleosides, [and] oligonucleotides” (column 7, lines 8-13). Thus, Kozlowski discloses PEG conjugates of amino acids as separate embodiments from PEG conjugates of biologically active agents such as small molecule drugs, nucleosides, and oligonucleotides. Kozlowski does not disclose an amino acid having the formula recited in amended claim 12, which requires, *inter alia*, at least two water-soluble polymer moieties *and* an  $R^{14}$  variable which is a nucleotide sugar (or comprises a saccharide moiety conjugated to a member selected from a peptide and a lipid) (emphasis added).

Moreover, Kozlowski discloses nucleosides (i.e., a base bound to five-carbon sugar) and oligonucleotides (i.e., a polymer of nucleotides) (see column 7, lines 8-13), but Kozlowski does not disclose an amino acid conjugate comprising “a nucleotide sugar” (i.e., a

base bound to a five-carbon sugar bound to one to three phosphate groups) as recited in definition "(b)" of the R<sup>14</sup> variable of amended claim 12.

Claim 22 as amended recites a pharmaceutical formulation comprising the amino acid according to claim 12 and a pharmaceutically acceptable carrier.

Since Kozlowski does not disclose the subject matter of claim 12 or the claims depending therefrom, the anticipation rejection based on Kozlowski should be withdrawn.


*Discussion of Rejection Under 35 U.S.C. § 103(a)*

Claims 14 and 15 have been rejected as allegedly obvious over Kozlowski in view of Sheridan. Claims 16-18, which were dependent on claim 12 either directly or indirectly, were not subject to the obviousness rejection. As indicated above, the elements of claims 16-18 essentially have been incorporated into claim 12, from which claims 14 and 15 are directly or indirectly dependent. Thus, the obviousness rejection has been rendered moot and should be withdrawn.

*Conclusion*

Applicant respectfully submits that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

  
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